Developing induced pluripotent stem cells into human therapeutics and disease models

Grant Award Details

Developing induced pluripotent stem cells into human therapeutics and disease models

Grant Type: Early Translational I

Grant Number: TR1-01277

Project Objective: Improve safety of hiPSC derived cell therapies - further detail is below under "Comments/other issues.

Investigator:

Name:	Yang Xu
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Diabetes, Metabolic Disorders

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $5,165,028

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Developing induced pluripotent stem cells into human therapeutics and disease models

Public Abstract: Human embryonic stem cells (hESCs) can undergo unlimited self-renewal and differentiate into all the cell types in the human body, and thus hold great promise for cell replacement therapy. However, one major problem for hESC-based therapy is that the cells derived from hESCs will be rejected by the recipient and can only be tolerated under persistent immunosuppression, which itself can cause cancer and infection. Recent development of induced pluripotent stem cells (iPSCs), which are generated from somatic cells of individual patient with defined factors and very similar to hESCs, could provide ideal cell source for transplantation by avoiding graft rejection in the patient. In addition, the disease-specific iPSCs can be used as human disease models for more reliable testing of the efficacy and toxicity of drugs. However, there are several major bottlenecks that prevent the development of iPSCs in human therapy and drug discovery. The overall goal of this proposal is to resolve the major bottlenecks remained in human iPSC biology to make it feasible for human therapy and drug discovery. We propose to develop safe and efficient approach to generate iPSCs from human patients. We propose to develop strategies to eliminate the risk of teratomas associated with the undifferentiated iPSCs. We propose to develop mouse model with functional human immune system to study the immune responses and tolerance during transplantation. Resolving these bottlenecks will greatly facilitate the development of hESCs into stem cell therapy and disease models for drug discovery.

Statement of Benefit to California: Diabetes and heart diseases remain the most costly diseases in our State and Nation. In the case of diabetes, 1 of every 10 Californians (2.7 million) were afflicted with diabetes in 2007, costing the State $24.5 billion annually. There is a significant increase in the occurrence of both types of diabetes in youths under 18 years of age (0.16% of youth <18 yr have type 1 diabetes nationally). Simply put, diabetes is having devastating consequences on both those afflicted and on State/National healthcare costs, and, given the staggering rise in both occurrence and costs, diabetes possesses the potential to completely overwhelm our healthcare system. There remains an urgent and critical need for a cell-based cure of diabetes. There is hope, since transplantation of functional β cells from human donors has been validated clinically to cure diabetes.

While significant progress has been made in the derivation of functional β cells and cardiomyocytes from human ES cells, these allogenic cells will be rejected by the recipient upon transplantation unless the immune system of the recipient is persistently suppressed. However, immune suppression itself has severe consequences with significantly increased risk of cancer and infection. This problem might be resolved by the recent breakthrough in induced pluripotent stem cell (iPSCs), which can be reprogrammed from somatic cells of human patients by defined factors and thus can provide a renewable source of autologous cells for transplantation. In addition, the disease-specific iPSCs will provide the much needed disease models to more reliably predict the drug responses in humans. With our significant progress in producing iPSCs without viral vectors or permanent genetic modification, our proposed research will resolve the major bottlenecks that hinder the development of iPSCs into human therapy and drug discovery. If successful, the funding spent now on research is nominal when compared to the billions that will be saved in treatment costs and the improved quality of life for patients.